

Appl. No. 09/700,712  
Amendment dated: March 22, 2006  
Reply to OA of: July 1, 2005

### **REMARKS**

Applicants have amended the claims to more particularly define the invention taking into consideration the outstanding Official Action which states that the proper identifier and underlining was not provided in claim 20 in the previous amendment. This amendment serves to correct this error.

The Remarks in the previous amendment are herein incorporated by reference and repeated as follows for the convenience of the Examiner.

As noted in the previous response, Applicants acknowledge with appreciation the telephone interview with Examiner Devi at which time the proposed amendments to claims 17, 18 and 23 were discussed. Corrected version of these amendments are included herein in an effort to overcome second paragraph 112 rejection. The amendments to the claims are fully supported by the specification and claim as originally filed.

In addition, new claims 24-29 have been added to specific aspects of the invention as also fully supported by the specification and claims as originally filed. Basis for claim 24 is found in the specification on page 6, lines 18-24. Basis for claim 25 is found in the specification on page 6, lines 25-29 and basis for claims 26 to 29 is in the experimental part of the specification. The claims now remaining in the application are claims 17-29. Applicant most respectfully submit that all of the claims now remaining in the application are in full compliance with 35 USC 112 and are clearly patentable over the references of record.

The rejection of claims 17-23 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention has been carefully considered but is most respectfully traversed in view of the above discussed amendments to these claims. In amending these claims it is believed that the various rejections under 35 USC 112 have been obviated. Accordingly, it is most respectfully requested that this rejection be withdrawn.

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It is most respectfully submitted that the objection to claims 18 and 23 have been obviated by the amendments to these claims. The Examiner's helpful comments are appreciated. Accordingly, it is most respectfully requested that these objections be withdrawn.

The rejection of claims 17-21 and 23 under 35 U.S.C. §102(b) as being anticipated by Morona et al. has been carefully considered but is most respectfully traversed in view of the amendments to the claims and the following comments.

Applicants acknowledge the telephone interview with Examiner Devi in connection with the outstanding rejection. During this interview it was pointed out by the undersigned attorney that the presently claimed invention relates to a synthetic strain of *Vibrio cholerae* and noted that the inserted gene in the Morona et al. is from *E. coli* and not from *Vibrio cholerae*.

Applicants most respectfully submit that one of ordinary in the art would fully appreciate that the cited reference to Morona et al. discusses a non-reverting thyA+ gene inserted into a plasmid which in turn may be inserted into a bacteria having a deficient thyA+ gene. A defective gene does not mean that it totally lacks its functionality as required in the present invention. On the other hand, the present invention concerns a non-reverting thyA- strain of *Vibrio cholerae* that has been deprived of its thyA functionality by selected nucleotide sequence deletion and/or insertion in the chromosome.

Applicants wish to direct the Examiner's attention to MPEP § 2131 which states that to anticipate a claim, the reference must teach every element of the claim.

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). "The identical invention must be shown in as complete detail as is contained in the ... claim." *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed Cir. 1989). The elements must be arranged as required by the claim, but this is not an *ipsissimis verbis* test, i.e., identity of

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terminology is not required. *In re Bond*, 910 F.2d 831, 15 USPQ2d 1566 (Fed.Cir. 1990).

Applicants do not believe that this standard has been met.

The Examiner specifically referred to the teaching at column 6 of the Monrona et al. reference which states the preselected bacterial strain for complementing with the *thyA* + gene, may be any suitable enteric bacteria. A salmonella strain or *Vibrio* strain may be utilized. It further states a strain of *Vibrio cholerae* may be utilized.

Example 4 at column 10, which the Examiner says teaches that the claimed invention has been produced in this reference has been carefully considered but is respectfully traversed. Where is the same language as claimed described in this example? Please clarify if this rejection is maintained. Applicants again wish to emphasize that the present claims relate to a delta *thyA* strain of *Vibrio cholerae* deprived of its *thyA* gene functionality but the Examiner repeatedly stated that this was disclosed in the reference. Clarification in the next Official Action by reference to the column and line number of the teaching in the reference would be appreciated and in the meantime the statement in the Official Action is specifically traversed.

Applicants again note the present specification, first page, lines 4, 5 discloses that the invention relates to a strain of *Vibrio cholerae* that has been deprived of its *thyA* gene in the chromosome, i.e. a  $\Delta$  *thyA* strain lacking the functionality of the *thyA* gene. Thus, Applicants are of the opinion that the " $\Delta$ " indicates that a man has made the strain that lacks the functionality of the *thyA* gene. It is believed that the Examiner agrees to this interpretation based on the undersign's telephone conversation with the Examiner. Applicants have previously enclosed a page 269 from the New England BioLabs Inc. 2005.05 Catalog & Technical References form which it is evident that a  $\Delta$  mutation present is known to be a large deletion.

Applicants have decided to concentrate this application to  $\Delta$  *thyA* mutants of *V. cholerae* that can be used as suitable production strains for recombinant proteins encoded on plasmids. (See specification page 1, lines 6-10, page 3, lines 2-6 and page

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5, lines 31, 32.) Accordingly, it is most respectfully requested that this rejection be withdrawn.

The rejection of claim 22 under 35 U.S.C. 103(a) as unpatentable over Morona et al. in view of Arntzen et al. has been carefully considered but is most respectfully traversed.

Applicants wish to direct the Examiner's attention to the basic requirements of a prima facie case of obviousness as set forth in the MPEP § 2143. This section states that to establish a prima facie case of obviousness, three basic criteria first must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine the reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations.

The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure. In re Vaeck, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

Section 2143.03 states that all claim limitations must be taught or suggested by the prior art. In re Royka, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). "All words in a claim must be considered in judging the patentability of that claim against the prior art." In re Wilson, 424 F.2d 1382, 1385, 165 USPQ 494, 496 (CCPA 1970). If an independent claim is nonobvious under 35 U.S.C. 103, then any claim depending therefrom is nonobvious. In re Fine, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988).

Applicants also most respectfully direct the Examiner's attention to MPEP § 2144.08 (page 2100-114) wherein it is stated that Office personnel should consider all rebuttal argument and evidence presented by applicant and the citation of In re Soni for error in not considering evidence presented in the specification.

The Examiner cites Morona et al. for the same reasons as applied in the anticipation rejection. However, for the above reasons, it is not believed that this rejection is tenable. Morona et al. discloses selection of mutant strains, i.e. point

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mutations in the strain and not defined *thyA* mutants of *Vibrio cholerae* as in the present case. As already discussed in the application, page 2, lines 6-16, the strains of Morona et al. may revert to wild-type at unacceptable high frequencies. Moreover, the necessary motivation is not found in the prior art and Applicants' specification may not be used as a teaching reference. Accordingly, it is most respectfully requested that these rejections be withdrawn.

In view of the above comments and further amendments to the claims, and for the reasons set forth in the previous response, favorable reconsideration and allowance of all of the claims now present in the application are most respectfully requested.

Respectfully submitted,

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